

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

IN THE CLAIMS:

Claim 53-56 have been canceled, without prejudice to prosecution in a continuing application, as a result of this amendment. Please note that all claims currently pending and under consideration in the referenced application are shown below. Please enter these claims as amended. This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

Claim 1 (currently amended): An isolated protein complex comprising two proteins, the protein complex selected from the group consisting of:

- (i) a complex of a first protein and a second protein;
- (ii) a complex of a fragment of said first protein and said second protein;
- (iii) a complex of said first protein and a fragment of said second protein; and
- (iv) a complex of a fragment of said first protein and a fragment of said second protein, wherein said first and second proteins of (i)-(iv) are selected from the group consisting of:
 - (a) said first protein is AKT1 and said second protein is selected from the group consisting of FNTA, TRPD, KIAA0728, PPL and Golgin-84;
 - (b) said first protein is AKT2 and said second protein is selected from the group consisting of CLIC1, AKR7A2 and TPRD; and
 - (c) said first protein is p90RSK and said second protein is selected from the group consisting of KIAA0728 and UNR.

Claim 2 (withdrawn): The protein complex of claim 1, wherein said protein complex comprises said first protein and said second protein.

Claim 3 (withdrawn): The protein complex of claim 1, wherein said protein complex comprises a fragment of said first protein and said second protein or said first protein and a fragment of said second protein.

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

Claim 4 (withdrawn): The protein complex of claim 1, wherein said protein complex comprises fragments of said first protein and said second protein.

Claim 5 (withdrawn): An isolated antibody selectively immunoreactive with a protein complex of claim 1.

Claim 6 (withdrawn): The antibody of claim 5, wherein said antibody is a monoclonal antibody.

Claim 7 (withdrawn): A method for diagnosing a physiological disorder in an animal, which comprises assaying for:

- (a) whether a protein complex set forth in claim 1 is present in a tissue extract;
- (b) the ability of proteins to form a protein complex set forth in claim 1; and
- (c) a mutation in a gene encoding a protein of a protein complex set forth in claim 1.

Claim 8 (withdrawn): The method of claim 7, wherein said animal is a human.

Claim 9 (withdrawn): The method of claim 8, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 10 (withdrawn): The method of claim 7, wherein the diagnosis is for a predisposition to said physiological disorder.

Claim 11 (withdrawn): The method of claim 7, wherein the diagnosis is for the existence of said physiological disorder.

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

Claim 12 (withdrawn): The method of claim 7, wherein said physiological disorder is selected from the group consisting neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 13 (withdrawn): The method of claim 7, wherein said assay comprises a yeast two-hybrid assay.

Claim 14 (withdrawn): The method of claim 7, wherein said assay comprises measuring *in vitro* a complex formed by combining the proteins of the protein complex, said proteins isolated from said animal.

Claim 15 (withdrawn): The method of claim 14, wherein said complex is measured by binding with an antibody specific for said complex.

Claim 16 (withdrawn): The method of claim 7, wherein said assay comprises mixing an antibody specific for said protein complex with a tissue extract from said animal and measuring the binding of said antibody.

Claim 17 (withdrawn): A method for determining whether a mutation in a gene encoding one of the proteins of a protein complex set forth in claim 1 is useful for diagnosing a physiological disorder, which comprises assaying for the ability of said protein with said mutation to form a complex with the other protein of said protein complex, wherein an inability to form said complex is indicative of said mutation being useful for diagnosing a physiological disorder.

Claim 18 (withdrawn): The method of claim 17, wherein said gene is an animal gene.

Claim 19 (withdrawn): The method of claim 18, wherein said animal is a human.

Appl. No. 10/035,344
Amtd. dated November 24, 2004
Reply to Office Action of August 24, 2004

Claim 20 (withdrawn): The method of claim 19, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 21 (withdrawn): The method of claim 17, wherein the diagnosis is for a predisposition to a physiological disorder.

Claim 22 (withdrawn): The method of claim 17, wherein the diagnosis is for the existence of a physiological disorder.

Claim 23 (withdrawn): The method of claim 17, wherein said assay comprises a yeast two-hybrid assay.

Claim 24 (withdrawn): The method of claim 17, wherein said assay comprises measuring *in vitro* a complex formed by combining the proteins of the protein complex, said proteins isolated from an animal.

Claim 25 (withdrawn): The method of claim 24, wherein said animal is a human.

Claim 26 (withdrawn): The method of claim 24, wherein said complex is measured by binding with an antibody specific for said complex.

Claim 27 (withdrawn): A non-human animal model for a physiological disorder wherein the genome of said animal or an ancestor thereof has been modified such that the formation of a protein complex set forth in claim 1 has been altered.

Claim 28 (withdrawn): The non-human animal model of claim 27, wherein said physiological disorder is selected from the group neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

Claim 29 (withdrawn): The non-human animal model of claim 27, wherein the formation of said protein complex has been altered as a result of:

- (a) over-expression of at least one of the proteins of said protein complex;
- (b) replacement of a gene for at least one of the proteins of said protein complex with gene from a second animal and expression of said protein;
- (c) expression of a mutant form of at least one of the proteins of said protein complex;
- (d) a lack of expression of at least one of the proteins of said protein complex; or
- (e) reduced expression of at least one of the proteins of said protein complex.

Claim 30 (withdrawn): A cell line obtained from the animal model of claim 27.

Claim 31 (withdrawn): A non-human animal model for a physiological disorder, wherein the biological activity of a protein complex set forth in claim 1 has been altered.

Claim 32 (withdrawn): The non-human animal model of claim 31, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 33 (withdrawn): The non-human animal model of claim 31, wherein said biological activity has been altered as a result of:

- (a) disrupting the formation of said complex; or
- (b) disrupting the action of said complex.

Claim 34 (withdrawn): The non-human animal model of claim 31, wherein the formation of said complex is disrupted by binding an antibody to at least one of the proteins which form said protein complex.

Claim 35 (withdrawn): The non-human animal model of claim 31, wherein the action of said complex is disrupted by binding an antibody to said complex.

AppL No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

Claim 36 (withdrawn): The non-human animal model of claim 31, wherein the formation of said complex is disrupted by binding a small molecule to at least one of the proteins which form said protein complex.

Claim 37 (withdrawn): The non-human animal model of claim 31, wherein the action of said complex is disrupted by binding a small molecule to said complex.

Claim 38 (withdrawn): A cell in which the genome of cells of said cell line has been modified to produce at least one protein complex set forth in claim 1.

Claim 39 (withdrawn): A cell line in which the genome of the cells of said cell line has been modified to eliminate at least one protein of a protein complex set forth in claim 1.

Claim 40 (withdrawn): A composition comprising:

 a first expression vector having a nucleic acid encoding a first protein or a homologue or derivative or fragment thereof; and

 a second expression vector having a nucleic acid encoding a second protein, or a homologue or derivative or fragment thereof, wherein said first and said second proteins are the proteins of claim 1.

Claim 41 (withdrawn): A host cell comprising:

 a first expression vector having a nucleic acid encoding a first protein which is first protein or a homologue or derivative or fragment thereof; and

 a second expression vector having a nucleic acid encoding a second protein which is second protein, or a homologue or derivative or fragment thereof, wherein said first and said second proteins are the proteins of claim 1.

Claim 42 (withdrawn): The host cell of claim 41, wherein said host cell is a yeast cell.

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

Claim 43 (withdrawn): The host cell of claim 41, wherein said first and second proteins are expressed in fusion proteins.

Claim 44 (withdrawn): The host cell of claim 41, wherein one of said first and second nucleic acids is linked to a nucleic acid encoding a DNA binding domain, and the other of said first and second nucleic acids is linked to a nucleic acid encoding a transcription-activation domain, whereby two fusion proteins can be produced in said host cell.

Claim 45 (withdrawn): The host cell of claim 41, further comprising a reporter gene, wherein the expression of the reporter gene is determined by the interaction between the first protein and the second protein.

Claim 46 (currently amended): A method for screening for drug candidates capable of modulating the interaction of the proteins of a protein complex, the protein complex selected from the group consisting of the protein complexes of claim 1, said method comprising comprising:

- (i) combining the proteins of said protein complex in the presence of a drug to form a first complex;
- (ii) combining the proteins in the absence of said drug to form a second complex;
- (iii) measuring the amount of said first complex and said second complex; and
- (iv) comparing the amount of said first complex with the amount of said second complex, wherein if the amount of said first complex is greater than, or less than the amount of said second complex, then the drug is a drug candidate for modulating the interaction of the proteins of said protein complex.

Claim 47 (original): The method of claim 46, wherein said screening is an *in vitro* screening.

Claim 48 (original): The method of claim 46, wherein said complex is measured by binding with an antibody specific for said protein complexes.

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

Claim 49 (original): The method of claim 46, wherein if the amount of said first complex is greater than the amount of said second complex, then said drug is a drug candidate for promoting the interaction of said proteins.

Claim 50 (original): The method of claim 46, wherein if the amount of said first complex is less than the amount of said second complex, then said drug is a drug candidate for inhibiting the interaction of said proteins.

Claim 51 (withdrawn): A drug useful for treating a physiological disorder identified by the method of claim 46.

Claim 52 (withdrawn): The drug of claim 51, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 53 (canceled)

Claim 54 (canceled)

Claim 55 (canceled)

Claim 56 (withdrawn): A method for selecting modulators of a protein complex formed between a first protein or a homologue or derivative or fragment thereof and a second protein or a homologue or derivative or fragment thereof, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

providing the protein complex;
contacting said protein complex with a test compound; and

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

determining the presence or absence of binding of said test compound to said protein complex.

Claim 57 (withdrawn): A modulator useful for treating a physiological disorder identified by the method of claim 56.

Claim 58 (withdrawn): The modulator of claim 57, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 59 (withdrawn): A method for selecting modulators of an interaction between a first protein and a second protein, said first protein or a homologue or derivative or fragment thereof and said second protein or a homologue or derivative or fragment thereof, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

contacting said first protein with said second protein in the presence of a test compound; and

determining the interaction between said first protein and said second protein.

Claim 60 (withdrawn): The method of claim 59, wherein at least one of said first and second proteins is a fusion protein having a detectable tag.

Claim 61 (withdrawn): The method of claim 59, wherein said step of determining the interaction between said first protein and said second protein is conducted in a substantially cell free environment.

Claim 62 (withdrawn): The method of claim 59, wherein the interaction between said first protein and said second protein is determined in a host cell.

Claim 63 (withdrawn): The method of claim 62, wherein said host cell is a yeast cell.

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

Claim 64 (withdrawn): The method of claim 59, wherein said test compound is provided in a phage display library.

Claim 65 (withdrawn): The method of claim 59, wherein said test compound is provided in a combinatorial library.

Claim 66 (withdrawn): A modulator useful for treating a physiological disorder identified by the method of claim 59.

Claim 67 (withdrawn): The modulator of claim 66, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 68 (withdrawn): A method for selecting modulators of a protein complex formed from a first protein or a homologue or derivative or fragment thereof, and a second protein or a homologue or derivative or fragment thereof, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

contacting said protein complex with a test compound; and
determining the interaction between said first protein and said second protein.

Claim 69 (withdrawn): A modulator useful for treating a physiological disorder identified by the method of claim 68.

Claim 70 (withdrawn): The modulator of claim 69, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

Claim 71 (withdrawn): A method for selecting modulators of an interaction between a first polypeptide and a second polypeptide, said first polypeptide being a first protein or a homologue or derivative or fragment thereof and said second polypeptide being a second protein or a homologue or derivative or fragment thereof, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

providing in a host cell a first fusion protein having said first polypeptide, and a second fusion protein having said second polypeptide, wherein a DNA binding domain is fused to one of said first and second polypeptides while a transcription-activating domain is fused to the other of said first and second polypeptides;

providing in said host cell a reporter gene, wherein the transcription of the reporter gene is determined by the interaction between the first polypeptide and the second polypeptide;

allowing said first and second fusion proteins to interact with each other within said host cell in the presence of a test compound; and

determining the presence or absence of expression of said reporter gene.

Claim 72 (withdrawn): The method of claim 71, wherein said host cell is a yeast cell.

Claim 73 (withdrawn): A modulator useful for treating a physiological disorder identified by the method of claim 71.

Claim 74 (withdrawn): The modulator of claim 73, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 75 (withdrawn): A method for identifying a compound that binds to a protein in vitro, wherein said protein is selected from the group consisting of the proteins of claim 1, said method comprising:

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

contacting a test compound with said protein for a time sufficient to form a complex and

detecting for the formation of a complex by detecting said protein or the compound in the complex,

so that if a complex is detected, a compound that binds to protein is identified.

Claim 76 (withdrawn): A compound useful for treating a physiological disorder identified by the method of claim 75.

Claim 77 (withdrawn): The compound of claim 76, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 78 (withdrawn): A method for selecting modulators of an interaction between a first polypeptide and a second polypeptide, said first polypeptide being a first protein or a homologue or derivative or fragment thereof and said second polypeptide being a second protein or a homologue or derivative or fragment thereof, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

providing atomic coordinates defining a three-dimensional structure of a protein complex formed by said first polypeptide and said second polypeptide; and

designing or selecting compounds capable of modulating the interaction between a first polypeptide and a second polypeptide based on said atomic coordinates.

Claim 79 (withdrawn): A modulator useful for treating a physiological disorder identified by the method of claim 78.

Claim 80 (withdrawn): The modulator of claim 79, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

Claim 81 (withdrawn): A method for providing inhibitors of an interaction between a first polypeptide and a second polypeptide, said first polypeptide being a first protein or a homologue or derivative or fragment thereof and said second polypeptide being a second protein or a homologue or derivative or fragment thereof, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:

providing atomic coordinates defining a three-dimensional structure of a protein complex formed by said first polypeptide and said second polypeptide; and

designing or selecting compounds capable of interfering with the interaction between a first polypeptide and a second polypeptide based on said atomic coordinates.

Claim 82 (withdrawn): An inhibitor useful for treating a physiological disorder identified by the method of claim 81.

Claim 83 (withdrawn): The inhibitor of claim 82, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 84 (withdrawn): A method for selecting modulators of a protein, wherein said protein is selected from the group consisting of the proteins of claim 1, said method comprising:

contacting said protein with a test compound; and
determining binding of said test compound to said protein.

Claim 85 (withdrawn): The method of claim 84, wherein said test compound is provided in a phage display library.

Claim 86 (withdrawn): The method of claim 84, wherein said test compound is provided in a combinatorial library.

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

Claim 87 (withdrawn): A modulator useful for treating a physiological disorder identified by the method of claim 84.

Claim 88 (withdrawn): The modulator of claim 87, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 89 (withdrawn): A method for modulating, in a cell, a protein complex having a first protein interacting with a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising:
administering to said cell a compound capable of modulating said protein complex.

Claim 90 (withdrawn): The method of claim 89, wherein said compound is selected from the group consisting of:

- (a) a compound which is capable of interfering with the interaction between said first protein and said second protein,
- (b) a compound which is capable of binding at least one of said first protein and said second protein,
- (c) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of said second protein and capable of binding said first protein,
- (d) a compound which comprises a peptide capable of binding said first protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of said second protein of the same length,
- (e) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of said first protein and capable of binding said second protein,

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

- (f) a compound which comprises a peptide capable of binding said second protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of said first protein of the same length,
- (g) a compound which is an antibody immunoreactive with said first protein or said second protein,
- (h) a compound which is a nucleic acid encoding an antibody immunoreactive with said first protein or said second protein,
- (i) a compound which modulates the expression of said first protein or said second protein,
- (j) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding said first protein or complement thereof, and
- (k) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding said second protein or complement thereof.

Claim 91 (withdrawn): A method for modulating, in a cell, a protein complex having a first protein interacting with a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, said method comprising: administering to said cell a peptide capable of interfering with the interaction between said first protein and said second protein, wherein said peptide is associated with a transporter capable of increasing cellular uptake of said peptide.

Claim 92 (withdrawn): The method of claim 91, wherein said peptide is covalently linked to said transporter which is selected from the group consisting of penetratins, *l*-Tat₄₉₋₅₇, *d*-Tat₄₉₋₅₇, retro-inverso isomers of *l*- or *d*-Tat₄₉₋₅₇, L-arginine oligomers, D-arginine oligomers, L-lysine oligomers, D-lysine oligomers, L-histidine oligomers, D-histidine oligomers, L-ornithine oligomers, D-ornithine oligomers, short peptide sequences derived from fibroblast growth factor, Galparan, and HSV-1 structural protein VP22, and peptoid analogs thereof.

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

Claim 93 (withdrawn): A method for modulating, in a cell, the interaction of a protein with a ligand, wherein said protein is selected from the group consisting of the first or second proteins of claim 1, said method comprising:

administering to said cell a compound capable of modulating said interaction.

Claim 94 (withdrawn): The method of claim 93, wherein said protein is one of said first or second proteins and said ligand is the other of said first or second proteins

Claim 95 (withdrawn): The method of claim 93, wherein said compound is selected from the group consisting of:

- (a) a compound which interferes with said interaction,
- (b) a compound which binds to said protein or said ligand,
- (c) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of said protein and capable of binding said ligand,
- (d) a compound which comprises a peptide capable of binding said ligand and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of said protein of the same length,
- (e) a compound which is an antibody immunoreactive with said protein or said ligand,
- (f) a compound which is a nucleic acid encoding an antibody immunoreactive with said ligand or said protein,
- (g) a compound which modulates the expression of said protein or said ligand, and
- (h) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding said ligand or said protein or complement thereof.

Claim 96 (withdrawn): A method for modulating neuronal death in a patient having a physiological disorder comprising:

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

modulating a protein complex having a first protein interacting with a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1.

Claim 97 (withdrawn): The method of claim 96, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 98 (withdrawn): A method for modulating neuronal death in a patient having physiological disorder comprising:

administering to the patient a compound capable of modulating a protein complex having a first protein interacting with a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1.

Claim 99 (withdrawn): The method of claim 98, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 100 (withdrawn): The method of claim 98, wherein said compound is selected from the group consisting of:

(a) a compound which is capable of interfering with the interaction between said first protein and said second protein,

(b) a compound which is capable of binding at least one of said first protein and said second protein,

(c) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of a second protein and capable of binding a first protein,

(d) a compound which comprises a peptide capable of binding a first protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of a second protein of the same length,

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

- (e) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of first protein and capable of binding a second protein,
- (f) a compound which comprises a peptide capable of binding a second protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of a first protein of the same length,
- (g) a compound which is an antibody immunoreactive with a first protein or a second protein,
- (h) a compound which is a nucleic acid encoding an antibody immunoreactive with a first protein or a second protein,
- (i) a compound which modulates the expression of a first protein or a second protein,
- (j) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding a first protein or complement thereof, and
- (j) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding a second protein or complement thereof

Claim 101 (withdrawn): A method for modulating neuronal death in a patient having physiological disorder comprising:

administering to said cell a peptide capable of interfering with the interaction between a first protein and a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, wherein said peptide is associated with a transporter capable of increasing cellular uptake of said peptide.

Claim 102 (withdrawn): The method of claim 101, wherein said peptide is covalently linked to said transporter which is selected from the group consisting of penetratins, *l*-Tat₄₉₋₅₇, *d*-Tat₄₉₋₅₇, retro-inverso isomers of *l*- or *d*-Tat₄₉₋₅₇, L-arginine oligomers, D-arginine oligomers, L-lysine oligomers, D-lysine oligomers, L-histidine oligomers, D-histidine oligomers, L-ornithine oligomers, D-ornithine oligomers, short peptide sequences derived from fibroblast growth factor, Galparan, and HSV-1 structural protein VP22, and peptoid analogs thereof.

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

Claim 103 (withdrawn): A method for treating a physiological disorder comprising: administering to a patient in need of treatment a compound capable of modulating a protein complex having a first protein interacting with a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1.

Claim 104 (withdrawn): The method of claim 103, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 105 (withdrawn): The method of claim 103, wherein said compound is selected from the group consisting of:

- (a) a compound which is capable of interfering with the interaction between said first protein and said second protein,
- (b) a compound which is capable of binding at least one of said first protein and said second protein,
- (c) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of said second protein and capable of binding said first protein,
- (d) a compound which comprises a peptide capable of binding said first protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of said second protein of the same length,
- (e) a compound which comprises a peptide having a contiguous span of amino acids of at least 4 amino acids of first protein and capable of binding said second protein,
- (f) a compound which comprises a peptide capable of binding said second protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of said first protein of the same length,
- (g) a compound which is an antibody immunoreactive with said first protein or said second protein,

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

- (h) a compound which is a nucleic acid encoding an antibody immunoreactive with said first protein or said second protein,
- (i) a compound which modulates the expression of said first protein or said second protein,
- (j) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding a first protein or complement thereof,
- (k) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding a second protein or complement thereof, and
- (l) a compound which is capable of strengthening the interaction between said first protein and said second protein.

Claim 106 (withdrawn): A method for treating a physiological disorder comprising: administering to said cell a peptide capable of interfering with the interaction between a first protein and a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1, wherein said peptide is associated with a transporter capable of increasing cellular uptake of said peptide.

Claim 107 (withdrawn): The method of claim 106, wherein said peptide is covalently linked to said transporter which is selected from the group consisting of penetratins, *l*-Tat₄₉₋₅₇, *d*-Tat₄₉₋₅₇, retro-inverso isomers of *l*- or *d*-Tat₄₉₋₅₇, L-arginine oligomers, D-arginine oligomers, L-lysine oligomers, D-lysine oligomers, L-histidine oligomers, D-histidine oligomers, L-ornithine oligomers, D-ornithine oligomers, short peptide sequences derived from fibroblast growth factor, Galparan, and HSV-1 structural protein VP22, and peptoid analogs thereof.

Claim 108 (withdrawn): The method of claim 106, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 109 (withdrawn): A method for treating a physiological disorder comprising:

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

administering to a patient in need of treatment a compound capable of modulating the activity of a first protein or a second protein, wherein said first and second proteins are selected from the group consisting of the proteins of claim 1.

Claim 110 (withdrawn): The method of claim 109, wherein said physiological disorder is selected from the group consisting of neuronal death, pancreatic cancer, glucose transport disorders and non-insulin dependent diabetes mellitus.

Claim 111 (withdrawn): The method of claim 109, wherein the activity is the interaction of said first protein or said second protein with a ligand.

Claim 112 (withdrawn): The method of claim 111, wherein said ligand is the other of said first or second protein.

Claim 113 (withdrawn): A method of modulating activity in a cell of a protein, said protein being first protein or a second protein selected from the group consisting of the proteins of claim 1, said method comprising:

administering to said cell a compound capable of modulating said protein.

Claim 114 (withdrawn): The method of claim 113, wherein said compound is selected from the group consisting of:

- (a) a compound which is capable of binding said protein,
- (b) a compound which comprises a peptide having a contiguous span of at least 4 amino acids of a first protein and capable of binding a second protein,
- (c) a compound which comprises a peptide capable of binding a second protein and having an amino acid sequence of from 4 to 30 amino acids that is at least 75% identical to a contiguous span of amino acids of a first protein of the same length,
- (d) a compound which is an antibody immunoreactive with said protein,
- (e) a compound which is a nucleic acid encoding an antibody immunoreactive with said protein, and

Appl. No. 10/035,344
Amdt. dated November 24, 2004
Reply to Office Action of August 24, 2004

(f) a compound which is an antisense compound or a ribozyme specifically hybridizing to a nucleic acid encoding said protein or complement thereof.

Claim 115 (withdrawn): A method for modulating activities of a protein in a cell, said protein being a first protein or a second protein selected from the group consisting of the proteins of claim 1, said method comprising:

administering to said cell a peptide having a contiguous span of at least 4 amino acids of one of said first or second proteins and capable of binding the other of said first or second proteins, wherein said peptide is associated with a transporter capable of increasing cellular uptake of said peptide.

Claim 116 (withdrawn): The method of claim 115, wherein said peptide is covalently linked to said transporter which is selected from the group consisting of penetratins, *L*-Tat₄₉₋₅₇, *d*-Tat₄₉₋₅₇, retro-inverso isomers of *L*- or *d*-Tat₄₉₋₅₇, L-arginine oligomers, D-arginine oligomers, L-lysine oligomers, D-lysine oligomers, L-histidine oligomers, D-histidine oligomers, L-ornithine oligomers, D-ornithine oligomers, short peptide sequences derived from fibroblast growth factor, Galparan, and HSV-1 structural protein VP22, and peptoid analogs thereof.